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EFFECT OF STAPHYLOCOCCAL ENTEROTOXIN B (SEB) ON CARDIORENAL FUN--ETC(U)
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Selected cardiovascular and renal functions were measured for 5 h in conscious, chair-restrained, female rhesus monkeys after intravenous (iv) (0.05 and 1.0 mg/kg) or oral (1.0 mg/kg) administration of staphylococcal enterotoxin B (SEB). Cardiovascular functions, renal hemodynamics, and renal metabolism were also studied between 6 and 11 h after iv SEB inoculation. Oral SEB produced few changes in cardiorenal functions. In contrast, iv SEB produced hypotension, tachycardia, increased total peripheral and renal vascular resistance, and decreased cardiac and renal functions. The early significant renal (cont'd)

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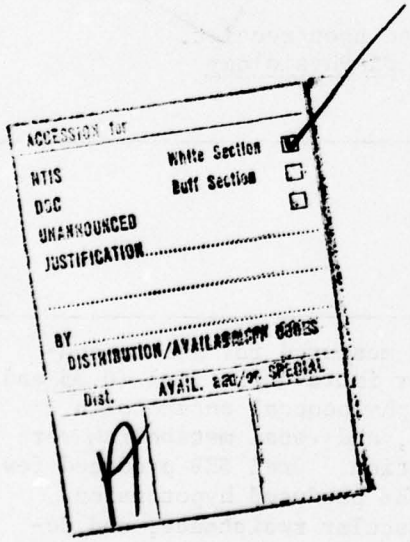
depression was not associated with hypotension (mean arterial blood pressure > 100 mm Hg). However, all measured renal functions except E_{PAH} were positively correlated with decreased blood pressure (r = 0.52 - 0.71) in the later phase of SEB toxemia. It is concluded that the kidney is one of the organs affected by iv SEB. Renal impairment may partially contribute to death during SEB enterotoxemia in monkeys.



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Running head: CARDIORENAL RESPONSES TO SEB IN MONKEYS

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ABSTRACT

Selected cardiovascular and renal functions were measured for 5 h in ~~conscious, chair-restrained,~~ female rhesus monkeys after intravenous (iv) (0.05 and 1.0 mg/kg) or oral (1.0 mg/kg) administration of staphylococcal enterotoxin B (SEB). Cardiovascular functions, renal hemodynamics, and renal metabolism were also studied between 6 and 11 h after iv SEB inoculation. Oral SEB produced few changes in cardiorenal functions. In contrast, iv SEB produced hypotension, tachycardia, increased total peripheral and renal vascular resistance, and decreased cardiac and renal functions. The early significant renal depression was not associated with hypotension (mean arterial blood pressure >100 mm Hg). However, all measured renal functions (except extraction ratio of PAH) E_{PAH} were positively correlated with decreased blood pressure ($r = 0.52 - 0.71$) in the later phase of SEB toxemia. It is concluded that the kidney is one of the organs affected by iv SEB. Renal impairment may partially contribute to death during SEB enterotoxemia in monkeys.

Key words: renal hemodynamics; renal metabolism; kidney and SEB; blood pressure vs. renal function.

EARLIER STUDIES in rabbits, cats and dogs have demonstrated that Staphylococcus aureus toxins produced glomerulonephritis and lesions of the endothelium in the small renal arteries, glomerular capillaries, peritubular capillary plexus, and tubular cells (23,28). Skinner and Hayes (25) showed a generalized renal depression with or without irreversible shock after iv injection of staphylococcus enterotoxin B (SEB) in dogs. The importance of the kidney in SEB toxemia in rabbits has been demonstrated by Israel et al. (7). These investigators showed that death was delayed when both kidneys were removed 7-10 h after a lethal dose of SEB. However, when bilateral nephrectomy was performed 3 h prior to SEB inoculation, survival time was significantly reduced. Similar results were also obtained in SEB-challenged monkeys (26).

Small quantities of SEB (25 μg/kg) are sufficient to produce shock and death in rhesus monkeys (3). Possible causes of death have been attributed to intracellular dehydration, hypovolemia (13), peripheral capillary blood pooling (1,4,22), endothelial cell damage (21), pulmonary edema (5,12,26,27), increased total peripheral resistance, and decreased cardiac functions (11).

The renal cortex was found to be the major site for radioiodinated SEB distribution in the monkey (17). Similar accumulations of fluorescein-labeled SEB were also found in the proximal tubules of the kidney in rats by Normann (14), who showed that SEB is filtered through the glomerular membranes and rapidly reabsorbed by the proximal tubular cells. Rapoport et al. (19) claimed that SEB may be metabolized in renal cells. Further, Canonico and associates (2) suggested that using rabbit kidney homogenates, SEB was pinocytized by renal tubular

cells. The objectives of this investigation were: 1) to study renal tubular, metabolic, and hemodynamic responses to iv inoculation of lethal doses of SEB in conscious rhesus monkeys, 2) to correlate renal changes with decreased mean arterial blood pressure (MABP) during the early and late period of SEB toxemia, and 3) to study renal responses to a large nonlethal dose of orally administered SEB (1 mg/kg).

MATERIALS AND METHODS

Apparently normal, healthy, female rhesus monkeys (Macaca mulatta) weighing 3-5 kg were used. A total of 98 macaques were allocated randomly into six groups and three subgroups within three of these (Table 1). Approximately 24 h before experiments, cannulas were introduced into the femoral artery and vein of monkeys anesthetized with halothane (10). For some monkeys (group IV), the left renal vein was also cannulated for renal hemodynamic and metabolic studies. All monkeys were conscious and chair-restrained during the period of experimentation.

Techniques for measurement of cardiovascular and renal functions including blood pressure, cardiac dynamics, total peripheral resistance, renal metabolism, renal concentrating capacity, acid-base balance, and renal handling of electrolytes were reported previously (10,11). Control base-line values were obtained from each monkey prior to SEB inoculation. Isotonic saline (1 ml) or highly purified SEB (24) (0.05 and 1.0 mg/kg) in saline was injected into the femoral vein via the catheter. Measurements were made hourly for a period of 5 h in monkeys from groups I, II and III. Hourly measurements on cardiorenal functions were also studied in group IV between 6 and 11 h after iv SEB inoculation. A large dose of SEB (1 mg/kg) was administered orally to group V

monkeys through a nasogastric tube. Control monkeys were given saline orally (group VI). Food was withheld from monkeys during the experimental period, but water was available ad libitum.

Statistical comparisons of the data using paired and independent t tests were made and standard errors of means were calculated. For data from 0-5 h after SEB (groups I, II, III, and VI), comparisons were made between differences from their own base-line values for both the control and SEB groups at any given time interval using an independent t test. For data between 6 and 11 h after SEB injection (group IV), paired t tests were employed using each monkey's own control values. Differences were considered significant at $P < 0.05$. Further, correlation coefficients for nine measured renal functions and MABP as a function of time (0-5 h, 6-11 h after iv SEB) were also calculated. Correlation was considered significant at $P < 0.01$.

RESULTS

Effect of iv SEB

Cardiovascular functions. Heart rate was significantly increased, while mean arterial blood pressure (MABP), cardiac output, stroke volume, and cardiac work were significantly decreased from base-line values after iv SEB administration (0.05 and 1.0 mg/kg) (Fig. 1 and 2). Total peripheral resistance increased 5 h after inoculation with a low dose of SEB (0.05 mg/kg), but little change was observed with a high dose of SEB (1 mg/kg) (Fig. 2). Reductions of cardiovascular functions were also observed during glucose and p-aminohippurate (PAH) loading in monkeys given iv SEB (groups IIb, IIc, IIIb and IIIc).

Renal hemodynamics. Effects of iv SEB on renal hemodynamics for a period of 11 h are summarized in Tables 2 and 3. Clearances of inulin (C_{in}) and PAH (C_{PAH}) decreased significantly 2 h after SEB; this was followed (within 60 min) by marked reductions of extraction ratio of PAH (E_{PAH}) total renal plasma flow, (TRPF), and total renal blood flow (TRBF), and increased renal resistance. However, significantly decreased filtration fraction (FF) values were not observed until 10 h after SEB. Renal fraction remained unaltered in group IIIa 5 h after SEB inoculation. Further, C_{PAH} calculated in terms of C_{in} (C_{PAH}/C_{in}), did not show significant changes for 11 h during the toxemia.

Renal metabolism. Within 11 h after SEB injection, renal O_2 consumption, CO_2 output, and respiratory quotient (RQ) showed few changes (Table 4 and 5). Arterial O_2 content was significantly decreased 5 h after the low dose of SEB (0.05 mg/kg). In monkeys receiving the high dose of SEB (1 mg/kg), arterial and renal venous O_2 content were significantly decreased at 8 to 11 h. Total CO_2 concentrations in the arterial and renal venous blood were also significantly decreased at 8-11 h. Total CO_2 concentrations in the arterial and renal venous blood were also significantly decreased 6-9 h after SEB inoculation. Although slight hypoglycemia and severe hypoproteinemia (4.9 g/100 ml) were found during SEB toxemia, no significant renal arteriovenous differences of glucose or protein were demonstrated (Table 5).

Blood and urine pH and gas tensions. Arterial and renal venous blood pH, PO_2, PCO_2, HCO_3^- and total CO_2 remained relatively constant during the 11 h experimental period following iv SEB challenge. In addition, renal arteriovenous differences of these variables did not

show significant changes. However, the urine pH decreased significantly from control values of 5.78 ± 0.14 to 5.26 ± 0.09 at 7 h, and reached 5.23 ± 0.14 at the end of the 11-h study. Further, urine PO_2 decreased from 52.4 ± 5.6 mm Hg to a lowest value of 40.0 ± 2.8 mm Hg between 6 and 11 h.

Renal concentrating capacity. Effects of SEB on renal concentrating capacity for a period of 11 h are presented in Tables 6 and 7. Arterial and renal venous plasma osmolalities increased significantly with constant glucose infusion between 3 and 5 h. No change was seen in plasma osmolality 6 h after iv SEB injection (no glucose load). Urine flow was reduced markedly between 6 and 11 h in the high dose group. Further, values for urine osmolality (U_{osm}) and tubular concentration of H_2O ($T^C_{H_2O}$) decreased significantly between 2 and 11 h after SEB inoculation. Monkeys receiving a low dose of SEB showed a biphasic response in urine osmolality; a significant decrease occurred between 2 and 3 h, but increased at 4-5 h post-SEB.

A significant decrease in the ratio of U_{osm} to plasma osmolality (P_{osm}) was found between 2 and 11 h in monkeys challenged with high doses of SEB (Table 7). When monkeys were inoculated with low doses of SEB, U_{osm}/P_{osm} values remained unaltered. No significant changes were observed in C_{osm}/C_{in} and $T^C_{H_2O}/C_{in}$ for the entire experimental period.

Renal maximal tubular activities. Changes in maximal renal tubular activities and ratio values of tubular maximal absorption of glucose (TmG) or PAH (TmPAH) to C_{in} and C_{PAH} for a period of 5 h in SEB monkeys are summarized in Table 8. Levels of TmG and TmG/C_{in} were maintained relatively constant throughout the experiment. TmPAH was significantly depressed at 2 and 5 h after iv injection of high

and low doses of SEB, respectively. The value for C_{in} in terms of TmG and TmPAH (C_{in}/TmG and C_{in}/TmPAH) decreased slightly after SEB. The TmPAH/C_{in} ratio increased significantly at 2-3 h. Insignificant changes were demonstrated on C_{in}/TmPAH, C_{PAH}/TmPAH, and TmG/C_{in} in SEB-challenged monkeys.

Renal handling of electrolytes. Plasma and urine concentrations of Na^+ and K^+ and renal handling of these ions within 5 h of iv SEB challenge are summarized in Tables 9 and 10. Plasma levels, excretory rate, and percent reabsorption of Na^+ did not show significant changes. However, the filtered load of Na^+ decreased markedly at 2-3 h. Plasma K^+ concentrations decreased significantly at the same time period, but returned to control levels at 4 h in the low dose group. The filtered load of K^+ decreased significantly at 2 h at a high or low dose challenge. Although a trend toward a decreased excretory rate of K^+ occurred in monkeys given low doses of SEB, severely reduced K^+ excretion was found in monkeys 4 h after inoculation of high doses of SEB. Renal handling of HCO_3^- and Cl^- was similar to that of Na^+ and no significant changes in plasma phosphorus levels and renal handling of phosphorus were observed.

Effects of glucose loading. Cardiovascular and renal functions were not significantly different between glucose-infused and nonglucose-infused rhesus monkeys following iv SEB injection. When base-line values of plasma glucose were elevated to 5.3 mg/ml by constant infusion of glucose, severe hyperglycemia (7.7 - 9.0 mg/ml) was observed at 2-3 h and the glucose level reached 13.2 mg/ml at 5 h (Table 11). However, in monkeys without glucose infusion, gradual hyperglycemia developed after injection of the low dose of SEB. In contrast, the high dose

of SEB produced significantly lowered glucose levels (0.71 mg/ml) 3 h post-SEB.

Correlation between renal function and MABP. Negative correlations were found between alterations of renal functions and decreased MABP during the early phase (0-5 h) of SEB toxemia (Table 12). However, the correlation coefficient (r) values were highly significant ($P < 0.01$) among renal functions (except E_{PAH}), 6 h after iv SEB injection (Table 13).

Effect of oral SEB. Selected renal responses to orally administered SEB (1 mg/kg) are shown in Table 14. There were no significant differences in measured renal functions in orally challenged monkeys (group V) compared to controls (group VI).

DISCUSSION

The evidence that renal functions remain unaltered after oral administration of SEB (1 mg/kg) is consistent with our previous findings that cardiovascular functions are unchanged in orally challenged monkeys (11). Data from the present study further support the hypothesis that orally administered SEB may not be transported in sufficient amount into the general circulation to exert significant systemic changes.

Hypotension, tachycardia, decrease in cardiac output, and increase in total peripheral resistance are common findings in monkeys after iv SEB inoculation (11). These cardiovascular changes were not modified significantly during constant infusion of fluid (1 ml/min) containing high concentrations of glucose, PAH, or mannitol for renal clearance studies (10). Although MABP was maintained at approximately 100 mm Hg for 5 h after iv SEB inoculation, (i.e., 25-30 mm Hg below base-line

values), minimal but statistically significant depression of several renal functions were produced. For example, C_{in}, C_{PAH}, TRPF, TRBF, and $T^{C}_{H_2O}$ were decreased 2-3 h post-SEB but did not correlate positively with decreased MABP. These findings provide the evidence that early renal changes during SEB toxemia are independent phenomena and should not be considered entirely as secondary responses to cardiovascular disturbances. However, drastic changes in renal function during the later period of SEB toxemia are largely associated with circulatory insufficiency or collapse. These positive correlations between renal functions and MABP were highly significant.

The distribution and fate of injected [^{131}I]SEB were studied by Rapoport et al. (20) and Normann and co-workers in monkeys and rats (15). Kidneys were found by them to be major organs for rapid removal of SEB from the blood. After both renal arteries were ligated in monkeys, the disappearance rate of the [^{131}I]SEB was markedly slowed (19).

Using fluorescein-labeled SEB in rats and monkeys, Normann et al. (15) observed that 75% of the injected label was accumulated rapidly in the proximal tubular cells, suggesting that the toxin was easily filtered through the glomeruli and reabsorbed at the proximal tubule. However, possible secretion of labeled SEB by the proximal tubule could not be excluded. If fluorescein dissociated from SEB molecules during the study, or if the kidneys handled it differently from SEB, the interpretation of Normann's data (15) may be open to question. If SEB could not be detected in the urine as he indicated, renal clearance of SEB would be 0 ml/min, and could not be considered as glomerular filtration rate (GFR).

Morris et al. (17) reported decreases in creatinine and PAH clearances with an increased urine flow for a period of 9 h after SEB challenge of anesthetized monkeys. Although these renal changes occurred simultaneously with a decline in mean arterial blood pressure, the magnitude of hypotension was not indicated. Further, these investigators claimed that SEB had no apparent direct effect on either glomerular or proximal tubular function. However, in the present study, the SEB-induced renal depression of C_{in}, C_{PAH}, TRPF, TRBF, and TmPAH occurred in the early phase of toxemia at a time when MABP was only 25 - 30 mm Hg below control baseline. Moreover, in the late period of SEB toxemia, E_{PAH} and urine flow decreased, and renal vascular resistance increased.

Renal lysosomal catabolism of SEB has been demonstrated in vitro by Normann and Stone (16) and Canonico et al. (2). It appears that some SEB may be destroyed slowly in the proximal tubules in vivo. In the present study, the iv injected SEB did exert certain renal toxic effects, which inhibited glomerular filtration, renal circulation, and renal tubular functions. However, there was a greater reduction of C_{in} as compared to renal tubular depression of TmG or TmPAH in the SEB-challenged monkeys, indicating that a condition of glumerulotubular imbalance was evident. In contrast, when decreased values of renal function (C_{PAH}, C_{osm}, $T^{C}_{H_2O}$) were expressed in terms of C_{in}, measured variables did not show significant changes from their pre-experimental base-line levels. These findings clearly indicate that decreased C_{in} is one of the key factors for modifying several renal functions. The possible causes for a decrease in C_{in} may be due to: 1) constriction of afferent arterioles, 2) severe simultaneous constriction of afferent

and efferent arterioles, 3) reduction of cardiac output and total renal flood flow, 4) decrease in glomerular capillary hydrostatic pressure, and/or 5) decrease in blood volume (13).

Since both C_{in} and urine flow decreased after iv SEB inoculation in monkeys, the filtered load and excretory rate for Na^+, K^+, HCO_3^- and Cl^- were also diminished. Consequently, the percent of renal reabsorption of Na^+, Cl^- and HCO_3^- remained unchanged. The question may be raised as to how hypokalemia was induced with a decreased rate of K^+ excretion. It appears the K^+ may be lost mainly from the gastrointestinal tract due to diarrhea and vomiting. Further, the SEB-induced transient hypokalemia with return to normal plasma K^+ levels suggest that cell membranes are maintained intact without a significant shift of intracellular K^+ into the extracellular space.

The urine-concentrating mechanisms of SEB-inoculated monkeys were strikingly impaired, as evidenced by significant reductions of urine osmolality, U_{osm}/P_{osm}, C_{osm} and $T^C_{H_2O}$. However, the degree of impairment was not as marked as the depression of renal hemodynamics. The decrease in $T^C_{H_2O}$ might result from a disturbance of the medullary osmotic gradient. Since E_{PAH} was markedly depressed post-SEB, the reduced medullary osmotic effects might be associated with a relative increase in renal medullary plasms flow (9). Further, when C_{in} is significantly decreased, fewer Na^+ and Cl^- ions are delivered to Henle's loop for active transport to the extracellular space of the kidney (8).

Certain biochemical changes during SEB toxemia in monkeys were studied by Crawley et al. (3), who showed decreased plasma protein and Cl^- concentrations and increased plasma phosphorus levels. These investigators also observed an initial modest hyperglycemia, followed

by slight hypoglycemia without changes in plasma Na^+ and K^+ concentrations. Data from the present study confirmed the findings of Crawley et al. (3) except that plasma Cl^- and phosphorus levels did not change significantly and hypokalemia developed in large-dose SEB-challenged monkeys.

Although arterial and renal venous blood PO_2 showed little change within 11 h after SEB injection, their O_2 and CO_2 contents were simultaneously reduced. Evidently, hypoxia and hypocapnia were associated with SEB toxicity. The finding of SEB-induced O_2 deficiency could be masked by measuring PO_2 alone without knowing the percent of hemoglobin saturation. However, Crawley et al. (3) showed an increased systemic arteriovenous difference of PO_2 during SEB toxemia in monkeys.

Renal O_2 consumption, CO_2 output, and RQ did not change significantly during the 11-h study. These data suggest that there was no significant change in renal work during the experimental period of toxemia. Consequently, the kidneys were able to conserve Na^+ and maintain nearly normal blood pH during the periods when most of the renal functions were impaired. Nevertheless, iv SEB-challenged monkeys excreted more acidified urine in which PO_2 values were also decreased.

Changes in plasma glucose levels were different between the two groups of SEB-challenged monkeys with or without glucose loading. After iv SEB injection, the glucose-loaded group showed progressive hyperglycemia during iv glucose infusion, while the group of monkeys without glucose loading responded with little change or slight hypoglycemia. The SEB-induced progressive hyperglycemia during glucose loading indicated that cellular utilization of glucose was impaired. This metabolic deficiency could not be demonstrated during SEB toxemia without glucose loading. Although glucose has been shown to be

effective in the treatment of endotoxemia in dogs (6) and experimental sepsis (18), results of the present study indicate that both clinical signs and survival were not significantly altered by constant glucose infusion during enterotoxemia in monkeys.

In conclusion, more sophisticated techniques have been used to clarify the problems of SEB-induced renal changes. During early iv SEB toxemia, renal changes are independent and are not associated with slightly decreased mean arterial blood pressure. Although renal depression or failure is not the direct cause of death of SEB-challenged monkeys (11,12) within 20 h, renal dysfunction potentiates the development of terminal acidosis and alters water and electrolyte metabolism. These biochemical changes may eventually impair functions of other vital organs (heart, lung and brain) and lead to death.

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In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on the Revision of the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Research Council. The facilities are fully accredited by the American Association for Accreditation of Laboratory Animal Care.

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TABLE 1. Random division of 98 rhesus monkeys for studying cardiorenal responses to intravenous and oral SEB

Group	Route	SEB Dose, mg/kg	Experimental Period, h	Variables Measured (Subgroup)	No. of Monkeys
I	iv	None	0-5	Cardiovascular and renal hemodynamics and metabolism (Subgroup a)	9
				Tubular maximal reabsorption of glucose (TmG) (Subgroup b)	10
				Tubular maximal secretion of p-aminohippurate (TmPAH) and handling of electrolytes (Subgroup c)	10
II	iv	0.05	0-5	Subgroup a	10
				Subgroup b	8
				Subgroup c	7
III	iv	1.0	0-5	Subgroup a	9
				Subgroup b	9
				Subgroup c	7
IV	iv	1.0	0, 6-11	subgroup a	10
V	Oral	1.0	0-5	TmPAH	6
VI	Oral	none	0-5	TmPAH	3

TABLE 2. Renal hemodynamics 1-5 h after intravenous SEB inoculation of groups Ia (n = 9), IIa (n = 8), and IIIa (n = 7)

Variable	Group	SEB, mg/kg	Value by Hours after SEB (± SE)					
			Baseline	1	2	3	4	5
C_{in}, ml/min/kg	Ia	0	3.80±0.21	3.49±0.21	3.49±0.18	3.47±0.17	3.50±0.17	3.44±0.29
	IIa	0.05	3.60±0.26	3.38±0.31	2.81±0.33*	2.49±0.38*	2.24±0.30*	2.26±0.43*
	IIIa	1.0	3.20±0.16	3.20±0.20	2.80±0.23*	2.70±0.21*	2.50±0.18*	2.40±0.20*
C_{PAH}, ml/min/kg	Ia	0	30.5±1.4	30.5±3.1	28.8±2.7	28.3±2.4	28.3±2.6	27.1±2.6
	IIa	0.05	29.3±3.2	26.9±3.0	21.2±2.9*	18.4±2.9*	17.4±2.4*	17.3±3.0*
	IIIa	1.0	30.6±2.2	27.7±2.2	22.5±2.1*	19.1±1.4*	17.5±1.0*	16.7±1.1*
Filtration fraction, %	Ia	0	12.4±0.9	11.9±0.6	13.3±0.9	13.3±0.7	13.3±0.7	13.7±0.6
	IIa	0.05	13.0±1.0	13.1±0.9	13.4±1.2	14.1±1.5	13.6±1.5	13.7±1.8
	IIIa	1.0	10.7±0.3	11.9±0.7	12.9±0.7	13.8±0.7	14.4±0.7	14.6±1.0
C_{PAH}/C_{in}	Ia	0	7.51±0.56	7.62±0.30	6.82±0.36	6.98±0.32	7.07±0.45	6.90±0.36
	IIa	0.05	8.32±0.90	7.86±0.54	7.34±0.50	7.46±0.84	7.81±0.87	8.11±1.23
	IIIa	1.0	9.42±0.30	8.44±0.51	7.97±0.51	7.39±0.40	7.10±0.39	7.12±0.56
E_{PAH}, %	Ia	0	91.2±1.3	92.7±1.0	93.1±0.7	93.2±0.9	92.2±0.9	92.0±1.0
	IIa	0.05	88.7±3.7	89.0±2.8	86.0±3.3	88.2±4.4	90.5±1.9	89.7±2.9
	IIIa	1.0	93.6±0.9	92.7±1.1	90.3±2.1	89.2±2.6*	84.0±4.4*	85.9±5.2

TABLE 2. Continued

TRPF, ml/min/kg	Ia	0	34.9±1.7	31.8±1.6	28.7±1.6	28.7±1.3	29.1±1.8	29.2±2.7
	IIa	0.05	34.0±5.1	30.5±3.8	25.0±3.6	20.5±2.7	18.8±2.5*	19.7±2.9*
	IIIa	1.0	34.4±2.9	31.4±2.7	25.9±2.4	22.3±1.6*	22.0±1.5*	20.7±1.6*
TRBF, ml/min/kg	Ia	0	51.2±2.4	45.8±2.2	40.9±2.2	40.4±1.8	40.3±2.5	40.2±3.6
	IIa	0.05	50.0±7.4	43.9±5.3	35.4±5.2	28.3±3.6*	25.6±3.3*	26.7±3.8*
	IIIa	1.0	49.4±3.7	44.8±3.8	36.3±3.2	30.8±1.6*	30.0±1.2*	28.2±2.2*
Renal resistance, (dyne·sec/cm^5)10^5	Ia	0	0.55±0.03	0.60±0.03	0.65±0.04	0.65±0.03	0.64±0.06	0.66±0.04
	IIa	0.05	0.54±0.07	0.63±0.09	0.80±0.16	0.94±0.16*	0.10±0.17*	0.95±0.16*
	IIIa	1.0	0.58±0.04	0.66±0.06	0.74±0.08	0.82±0.05*	0.81±0.04*	0.88±0.06*
Renal fraction, %	Ia	0	20.0±2.5	--	--	--	--	16.5±2.5
	IIa	0.05	22.9±4.4	--	--	--	--	13.7±1.3
	IIIa	1.0	14.6±1.9	--	--	--	--	10.3±1.0

* $P < 0.05$ by independent t test of differences.

TABLE 3. Renal hemodynamics 6-11 h after intravenous SEB inoculation (1 mg/kg) for group IV (n = 10)

Variable	Values by hours after SEB (±SE)						
	Baseline	6	7	8	9	10	11
C_{in}, ml/min/kg	3.68±0.28	1.69±0.32*	1.38±0.32*	1.19±0.27*	1.03±0.27*	0.93±0.26*	0.86±0.25*
C_{PAH}, ml/min/kg	29.7±4.1	12.2±1.6*	12.3±1.7*	11.6±1.7*	11.1±1.6*	12.6±1.5*	10.5±1.4*
FF, %	13.7±1.0	15.8±2.3	12.1±2.2	11.5±1.8	9.68±1.90	6.49±1.38*	6.86±1.34*
E_{PAH}, %	94.6±0.4	74.2±8.2*	73.9±8.3*	77.0±7.8*	73.9±7.7*	68.6±6.9*	71.9±8.2*
TRPF, ml/min/kg	31.7±4.3	16.2±2.0*	16.4±2.3*	15.1±3.0*	15.7±3.0*	18.9±4.3*	16.4±3.4*
TRBF, ml/min/kg	46.9±6.5	23.0±2.7*	23.0±3.1*	20.0±3.9*	21.1±3.9*	24.7±5.3*	22.7±3.9*
Renal resistance, $(dynes \cdot sec/cm^5)10^5$	0.61±0.07	0.89±0.07*	0.96±0.11*	0.90±0.11*	0.90±0.16	0.72±0.14	0.90±0.21
C_{PAH}/C_{in}	7.7±0.6	9.3±1.7	15.3±3.9	19.3±3.3	35.3±17.7	77.3±41.0	87.2±52.3

* $P < 0.05$ compared to baseline.

TABLE 4. Renal O_2 consumption, CO_2 output, and RQ 1-5 h after intravenous SEB inoculation for groups Ia (n = 5) and IIa (n = 8)

Variable	Group	SEB, mg/kg	Value by Hours after SEB (± SE)					
			Baseline	1	2	3	4	5
Arterial O_2 content, vol %	Ia	0	13.2±0.4	12.5±0.4	11.6±0.8	12.0±0.8	11.1±0.4	10.6±0.5
	IIa	0.05	10.9±0.5	10.7±0.4	10.3±0.4	9.5±0.4	9.4±0.4	8.9±0.4*
Renal venous O_2 content, vol %	Ia	0	10.8±0.5	10.2±0.4	9.6±0.6	9.0±0.7	8.6±0.4	7.8±0.6
	IIa	0.05	8.7±0.6	8.7±0.4	7.1±0.6	6.7±0.6	6.2±0.6	5.6±0.6
Renal O_2 consumption, $L/h/m^2$	Ia	0	0.98±0.17	0.94±0.12	0.90±0.12	1.11±0.12	0.94±0.09	1.03±0.13
	IIa	0.05	1.03±0.17	0.83±0.20	0.99±0.11	0.66±0.08	0.71±0.03	0.73±0.08
Arterial O_2 content, mM/L	Ia	0	16.7±2.8	15.7±2.9	17.2±2.4	18.6±2.0	15.6±3.5	15.2±3.4
	IIa	0.05	15.4±2.2	13.5±1.7	14.4±1.7	12.8±1.0	12.3±0.8	12.9±1.3
Renal venous O_2 content, mM/L	Ia	0	19.3±2.9	18.5±2.7	19.4±2.9	19.9±2.4	19.6±3.2	19.5±2.5
	IIa	0.05	17.4±2.4	16.8±1.1	15.4±1.5	16.2±1.2	14.0±0.8	16.0±0.7
Renal CO_2 output, $L/h/m^2$	Ia	0	2.75±0.63	2.62±0.26	4.65±1.68	2.60±0.66	3.02±0.81	3.37±0.99
	IIa	0.05	2.11±0.72	2.06±0.57	2.13±0.47	2.56±0.57	2.06±0.37	1.98±0.55
Renal RQ	Ia	0	2.02±0.91	1.87±0.30	2.95±0.81	1.40±0.33	1.85±0.37	2.85±0.19
	IIa	0.05	1.64±0.81	2.77±1.10	1.57±0.39	3.15±0.94*	1.80±0.50	2.05±0.59

P < 0.05 by independent t test of differences.

TABLE 5. Arterial and renal venous concentrations of glucose and protein, and renal metabolism 6-11 h after intravenous SEB inoculation (1 mg/kg) for group IV (n = 8)

Variable	Values by Hours after SEB (± SE)						
	Baseline	6	7	8	9	10	11
Arterial O_2 content, vol %	11.9±0.7	11.4±0.5	10.7±0.5	9.8±0.5*	9.3±0.5*	9.0±0.5*	8.6±0.4*
Renal venous O_2 content, vol %	10.0±0.7	7.7±0.7	6.7±0.6*	6.6±0.8*	6.4±0.8*	6.2±0.5*	6.1±0.6*
Renal O_2 consumption, $L/h/m^2$	1.14±0.25	1.02±0.12	1.01±0.17	0.60±0.08	1.03±0.49	1.39±0.43	1.43±0.75
Arterial CO_2, mM/L	16.9±0.9	14.0±0.8*	13.5±0.9*	12.9±0.8*	13.2±0.9	13.0±0.7*	13.3±0.8*
Renal venous CO_2, mM/L	19.8±1.1	16.9±1.2	17.5±1.5	16.3±0.4	16.0±1.2*	16.1±1.4*	15.9±1.1*
Renal CO_2 output, $L/h/m^2$	3.04±0.50	1.70±0.45	2.33±0.63	1.73±0.56	2.09±0.52	3.10±0.98	2.47±0.97
Renal RQ	3.27±0.48	2.49±0.83	1.31±0.34*	2.72±0.78	1.97±0.36	2.08±0.40	1.97±0.40
Arterial plasma glucose, mg/ml	1.13±0.07	0.98±0.07	0.96±0.07	1.05±0.10	1.03±0.08	0.96±0.08	0.94±0.07
Renal venous plasma glucose, mg/ml	1.30±0.07	1.01±0.06*	1.00±0.06*	1.05±0.09	1.03±0.07*	0.91±0.06*	0.84±0.08*
Arterial plasma protein, g/100 ml	6.23±0.17	5.68±0.19	5.51±0.16*	5.36±0.15*	5.20±0.16*	5.08±0.15*	5.00±0.15*
Renal venous plasma protein, g/100 ml	6.16±0.17	5.46±0.18*	5.36±0.16*	5.23±0.17*	5.04±0.18*	4.96±0.15*	4.85±0.16*

* $P < 0.05$ compared to baseline.

TABLE 6. Renal concentrating capacity 1-5 h after intravenous SEB inoculation for groups Ib (n = 10), IIb (n = 8) and IIIb (n = 9) during a constant glucose infusion of 450 mg/kg

Variable	Group	SEB, mg/kg	Value by Hours after SEB (± SE)					
			Baseline	1	2	3	4	5
Arterial plasma osmolality, mOsm/kg	Ib	0	302±2	301±2	300±2	299±2	298±1	297±2
	IIb	0.05	302±3	303±3	303±2	305±3	309±3*	310±3*
	IIIb	1.0	305±1	303±2	305±2	308±2*	307±2*	306±1*
Renal venous plasma osmolality, mOsm/kg	Ib	0	303±2	300±2	300±2	298±2	297±1	297±2
	IIb	0.05	304±3	305±2*	306±3*	308±3*	308±3*	309±4*
	IIIb	1.0	303±2	301±1	305±1*	306±1*	306±2*	306±2*
Urine osmolality, mOsm/L	Ib	0	528±23	548±16	557±17	564±16	559±15	516±15
	IIb	0.05	440±25	467±20	438±17*	424±24*	457±22*	459±20*
	IIIb	1.0	567±32	540±14	480±17*	459±16*	488±14*	505±14*
Urine flow, ml/min	Ib	0	0.71±0.04	0.66±0.02	0.65±0.02	0.66±0.03	0.67±0.03	0.66±0.05
	IIb	0.05	0.93±0.10	0.83±0.08	0.74±0.09	0.73±0.08	0.64±0.06*	0.60±0.05*
	IIIb	1.0	0.71±0.06	0.68±0.02	0.69±0.02	0.70±0.02	0.67±0.02	0.62±0.02
C_{osm}, ml/min/kg	Ib	0	0.34±0.01	0.33±0.01	0.34±0.01	0.34±0.01	0.35±0.01	0.34±0.02
	IIb	0.05	0.35±0.02	0.34±0.03	0.29±0.03*	0.27±0.03*	0.25±0.03*	0.24±0.03*
	IIIb	1.0	0.36±0.01	0.34±0.01	0.31±0.01*	0.30±0.01*	0.30±0.01*	0.29±0.01*

TABLE 6. Continued

$T^C_{H_2O}$, ml/min/kg	Ib	0	0.14±0.01	0.15±0.01	0.16±0.01	0.16±0.01	0.16±0.01	0.16±0.01
	IIb	0.05	0.11±0.01	0.12±0.01	0.09±0.01*	0.07±0.02*	0.08±0.01*	0.08±0.01*
	IIIb	1.0	0.16±0.01	0.15±0.01	0.11±0.01*	0.10±0.01*	0.11±0.01*	0.11±0.01*
U_{osm}/P_{osm}	Ib	0	1.75±0.07	1.82±0.05	1.86±0.06	1.89±0.06	1.87±0.05	1.89±0.05
	IIb	0.05	1.45±0.07	1.54±0.06	1.44±0.06	1.39±0.08	1.53±0.08	1.48±0.07
	IIIb	1.0	1.86±0.11	1.78±0.05	1.58±0.05*	1.49±0.05*	1.59±0.05*	1.65±0.05*
C_{osm}/C_{in}	Ib	0	0.09±0.01	0.10±0.01	0.10±0.01	0.10±0.01	0.10±0.01	0.10±0.01
	IIb	0.05	0.10±0.01	0.10±0.01	0.10±0.01	0.11±0.01	0.11±0.01	0.12±0.01
	IIIb	1.0	0.11±0.01	0.11±0.01	0.11±0.01	0.12±0.01	0.13±0.01	0.13±0.01
$T^C_{H_2O}/C_{in}$	Ib	0	0.034±0.005	0.041±0.002	0.046±0.003	0.045±0.001	0.047±0.001	0.045±0.003
	IIb	0.05	0.029±0.004	0.033±0.004	0.031±0.004	0.029±0.006	0.032±0.006	0.036±0.006
	IIIb	1.0	0.050±0.003	0.046±0.002	0.040±0.003	0.037±0.002	0.044±0.002	0.048±0.003

$P < 0.05$ by independent t test of differences.

TABLE 7. Renal concentrating capacity 6-11 h after intravenous SEB inoculation (1 mg/kg) for group IV (n = 10)

Variable	Values by Hours after SEB (±SE)						
	Baseline	6	7	8	9	10	11
Arterial plasma osmolality, mOsm/kg	300± 2	304± 4	305± 5	305± 5	308± 6	307± 6	309± 6
Renal venous plasma osmolality, mOsm/kg	300± 3	306± 4	306± 5	307± 5	308± 6	310± 7	308± 7
Urine osmolality, mOsm/kg	540±25	505±21	474±19	451±18*	429±18*	408±16*	401±17*
Urine flow, ml/min	0.93±0.09	0.44±0.06*	0.43±0.06*	0.43±0.07*	0.40±0.08*	0.40±0.08*	0.41±0.09*
C_{osm}, ml/min/kg	0.40±0.04	0.21±0.30*	0.20±0.03*	0.19±0.04*	0.17±0.03*	0.17±0.03*	0.18±0.04*
$T^C_{H_2O}$, ml/min/kg	0.186±0.020	0.112±0.013*	0.100±0.011*	0.093±0.010*	0.087±0.044*	0.046±0.013*	0.043±0.014*
U_{osm}/P_{osm}	1.80±0.08	1.66±0.07	1.56±0.07*	1.48±0.07*	1.40±0.07*	1.34±0.07*	1.31±0.07*
$T^C_{H_2O}/C_{in}$	0.046±0.004	0.048±0.004	0.061±0.015	0.047±0.006	0.048±0.003	0.046±0.003	0.049±0.003
C_{osm}/C_{in}	0.14±0.04	0.13±0.01	0.20±0.06	0.18±0.02	0.23±0.04	0.31±0.08	0.38±0.11

* $P < 0.05$ compared to baseline.

TABLE 8. Renal maximal tubular activities 1-5 h after intravenous SEB inoculation for groups Ib (n = 9), IIb (n = 8), IIIb (n = 7), Ic (n = 10), IIc (n = 7), and IIIc (n = 7)

Variable	Group	SEB, mg/kg	Value by Hours after SEB (± SE)					
			Baseline	1	2	3	4	5
TmG, mg/min/kg	Ib	0	5.31±0.65	6.42±0.72	7.58±0.63	6.71±1.20	6.59±0.94	7.78±1.10
	IIb	0.05	6.18±0.65	6.18±0.78	6.32±0.93*	7.48±1.01	7.25±1.41	10.2 ±1.63
	IIIb	1.0	9.59±2.10	9.11±2.70	9.33±1.47	8.50±1.78	6.49±1.56*	9.11±0.93
Tm_{PAH}, mg/min/kg	Ic	0	4.02±0.30	3.95±0.36	4.05±0.31	3.93±0.29	3.93±0.30	3.92±0.32
	IIc	0.05	4.20±0.32	4.18±0.32	4.01±0.25	3.90±0.23	3.63±0.21	3.41±0.21*
	IIIc	1.0	3.82±0.11	3.59±0.25	3.02±0.38*	2.91±0.42*	3.25±0.22	3.07±0.26*
TmG/C_{in}	Ib	0	1.55±0.18	1.89±0.16	2.18±0.20	2.04±0.37	1.96±0.34	2.30±0.39
	IIb	0.05	1.71±0.19	1.77±0.22	2.13±0.37	2.74±0.34	2.65±0.44	3.61±0.49
	IIIb	1.0	2.66±0.53	2.70±0.76	3.54±0.50	4.04±0.55	3.40±0.85	4.95±1.12
Tm_{PAH}/C_{in}	Ic	0	1.52±0.11	1.47±0.10	1.41±0.12	1.43±0.08	1.38±0.08	1.35±0.10
	IIc	0.05	1.46±0.09	1.44±0.06	1.51±0.09	1.72±0.15*	1.76±0.13*	1.90±0.20*
	IIIc	1.0	1.36±0.08	1.29±0.12	1.69±0.23*	3.09±1.03*	3.64±1.35*	4.63±1.73*
C_{in}/TmG	Ib	0	0.67±0.05	0.57±0.06	0.49±0.04	0.61±0.08	0.62±0.09	0.56±0.13
	IIb	0.05	0.67±0.08	0.66±0.08	0.61±0.13	0.43±0.08	0.48±0.07	0.27±0.04
	IIIb	1.0	0.58±0.09	0.77±0.30	0.37±0.05	0.34±0.05	0.78±0.40	0.24±0.06

TABLE 8. Continued

C_{PAH}/TmG	Ib	0	6.28±0.78	5.48±0.89	4.00±0.67	5.14±0.97	4.80±1.06	5.38±2.04
	IIb	0.05	5.11±0.79	4.53±0.50	3.95±0.72	2.71±0.42	2.72±0.56	1.75±0.17
	IIIb	1.0	3.93±0.86	3.80±0.64	3.26±0.51	3.31±0.57	3.57±0.98	1.82±0.31
C_{in}/Tm_{PAH}	Ic	0	0.70±0.06	0.71±0.05	0.71±0.06	0.72±0.05	0.75±0.05	0.75±0.05
	IIc	0.05	0.69±0.05	0.71±0.03	0.68±0.04	0.62±0.05	0.61±0.05*	0.58±0.06
	IIIc	1.0	0.75±0.04	0.81±0.08	0.64±0.06*	0.47±0.08*	0.51±0.10*	0.50±0.09*
C_{PAH}/Tm_{PAH}	Ic	0	7.09±0.48	6.87±0.40	6.04±0.67	6.21±0.45	6.22±0.37	7.17±0.91
	IIc	0.05	8.27±0.53	7.37±1.35	5.90±1.05	5.26±1.00	5.34±0.98	5.79±1.20
	IIIc	1.0	6.87±0.53	6.97±0.82	7.96±1.54	7.35±1.74	4.89±0.29	4.88±0.43

P < 0.05 by independent t test of differences.

TABLE 9. Plasma and urine concentrations of Na^+ and renal handling of Na^+ after intravenous SEB inoculation for groups Ic (n = 7), IIc (n = 5) and IIIc (n = 7)

Group (SEB dose, mg/kg)	Variable	Value by Hours after SEB (± SE)					
		Baseline	1	2	3	4	5
Ic (0)	Plasma, meq/L	139±2	138±1	139±2	137±1	136±2	139±2
	Urine, meq/L	87.5±4.8	74.5±5.5	81.5±7.3	71.1±4.6	73.6±3.0	69.8±2.2
	FL, meq/min	1.45±0.10	1.47±0.14	1.45±0.09	1.44±0.10	1.49±0.10	1.45±0.11
	ER, μeq/min	89±14	75±10	93±25	72± 9	78±14	61± 3
	Reabsorption, %	94.2±0.8	95.5±0.9	93.6±1.6	95.0±0.6	94.8±0.7	95.7±0.3
IIc (0.05)	Plasma, meq/L	140±1	142±2	138±1	139±1	139±1	140±1
	Urine, meq/L	83.1±5.7	69.1±2.9	63.6±3.7	72.5±5.7	69.4±1.9	70.6±2.7
	FL, meq/min	1.49±0.11	1.51±0.11	1.37±0.11	1.25±0.12*	1.20±0.13	1.08±0.16*
	ER, μeq/min	74±6	66±8	56±6	66±7	56±6	57±8
	Reabsorption, %	95.0±0.1	95.9±0.5	96.0±0.3	94.5±0.5	94.9±0.8	94.6±1.0
IIIc (1.0)	Plasma, meq/L	140±1	142±2	138±1	139±1	140±1	141±1
	Urine, meq/L	80.1±6.9	65.3±5.8	63.6±4.4	68.7±7.8	66.2±7.7	71.3±6.2
	FL, meq/min	1.65±0.07	1.64±0.13	1.14+0.19*	0.84±0.20*	0.92±0.17*	0.85±0.18*
	ER, μeq/min	93±18	72± 9	54± 6	52± 9	66± 8	66± 9
	Reabsorption, %	94.5±1.2	95.3±1.1	95.4±0.3	90.2±3.5	90.3±3.5	89.3±3.4*

FL, filtered load; ER, excretory rate.

$P < 0.05$ by independent t test of differences.

TABLE 10. Plasma and urine concentrations of K^+ and renal handling of K^+ after intravenous SEB inoculation for groups Ic (n = 7), IIc (n = 5) and IIIc (n = 7)

Group (SEB dose, mg/kg)	Variable	Value by Hours after SEB (± SE)					
		Baseline	1	2	3	4	5
Ic (0)	Plasma, meq/L	2.90±0.22	2.95±0.15	2.92±0.17	2.87±0.16	2.80±0.08	2.90±0.07
	Urine, meq/L	27.2±4.4	24.5±3.9	28.5±4.1	23.6±3.4	25.3±3.2	24.8±3.2
	FL, μeq/min	29.5±2.4	29.1±2.8	28.8±2.3	28.8±2.3	30.3±2.5	28.4±2.6
	ER, μeq/min	27.7±3.4	25.0±2.4	29.2±6.6	25.0±2.3	27.3±5.1	22.8±1.8
IIc (0.05)	Plasma, meq/L	3.04±0.10	3.12±0.10	2.48±0.11*	2.48±0.08*	2.70±0.04	2.72±0.14
	Urine, meq/L	23.1±3.0	21.8±2.4	20.5±2.1	18.6±1.1	17.0±0.8	18.8±1.1
	FL, μeq/min	29.2±2.6	29.7±3.3	22.5±1.9*	21.6±3.1*	21.8±3.5*	19.5±2.4*
	ER μeq/min	18.9±3.0	20.3±3.0*	17.7±2.7	17.4±1.6	14.4±0.6	15.5±1.6
IIIc (1.0)	Plasma, meq/L	3.04±0.10	3.12±0.10	2.48±0.12*	2.48±0.09*	2.70±0.04*	2.72±0.14
	Urine, meq/L	28.0±2.9	25.6±2.4	24.1±2.2	23.0±2.4	17.2±2.1	18.7±1.8
	FL, μeq/min	38.0±3.4	33.0±2.7	19.0±3.7*	16.8±3.5*	17.9±3.2*	17.6±3.4*
	ER, μeq/min	28.2±1.8	28.6±2.2	21.6±3.1	17.7±3.0	17.5±1.8*	17.3±1.8*

FL, filtered load; ER, excretory rate.

$P < 0.05$ by independent t test of differences.

TABLE 11. Changes in arterial plasma glucose concentration with or without glucose loading in intravenous SEB-inoculated monkeys

Group	(n)	SEB, mg/kg	mg/ml Glucose by Hours after SEB (± SE)					
			Baseline	1	2	3	4	5
Glucose	Ib (5)	0	4.90±0.77	5.34±0.78	5.94±0.93	5.65±0.91	5.48±1.10	4.57±0.75
load	IIb (10)	0.05	5.25±0.35	5.58±0.41	6.83±0.48	7.88±0.62*	8.63±0.79*	9.76±1.10*
	IIIb (7)	1.0	5.33±0.33	6.02±0.35	7.74±0.61*	9.01±0.89*	10.7 ±1.20*	13.2 ±2.20*
No	Ia (9)	0	0.78±0.04	0.79±0.03	0.83±0.03	0.83±0.04	0.92±0.06	0.98±0.06
glucose	IIa (8)	0.05	0.76±0.04	0.77±0.05	0.87±0.04	0.84±0.04	0.93±0.05	1.00±0.10
load	IIIa (9)	1.0	0.87±0.04	0.88±0.04	0.89±0.07	0.71±0.04*	0.79±0.04*	0.87±0.06

Continuous glucose infusion of 45 mg/min/kg after a priming dose of 450 mg/kg.

$P < 0.05$ by independent t test of differences.

TABLE 12. Correlation coefficients of renal functions vs. mean arterial blood pressure (MABP) during early phase (0-5 h) of SEB toxemia

MABP vs.	Correlation Coefficient		
	Control	SEB	
		0.05 mg/kg	1.0 mg/kg
TmG	- 0.160	0.194	0.039
Tm_{PAH}	0.241	0.298	0.148
C_{in}	- 0.205	0.242	0.152
C_{PAH}	0.314	- 0.016	0.211
TRPF	0.311	0.061	0.181
TRBF	0.296	0.111	0.315
E_{PAH}	0.125	- 0.319	- 0.103
C_{osm}	0.089	0.130	0.288
$T^{C}_{H_2O}$	0.067	- 0.041	- 0.303

Correlation coefficents are not significant.

TABLE 13. Correlation coefficients of renal functions vs. mean arterial blood pressure (MABP) during late phase (6-11 h) of SEB toxemia

MABP vs.	Correlation coefficient	P Value
C_{in}	0.708	< 0.01
C_{PAH}	0.535	< 0.01
TRPF	0.522	< 0.01
TRBF	0.463	< 0.01
E_{PAH}	0.237	Not significant
C_{osm}	0.661	< 0.01
$T^{C}_{H_2O}$	0.532	< 0.01

TABLE 14. Selected renal responses to orally administered SEB (1 mg/kg) (n = 6) and controls (n = 3)

Variable	Group	Value by Hours after SEB (± SE)			
		Baseline	1	3	5
C_{in}, ml/min/kg	Controls	2.46±0.45	2.76±0.45	2.80±0.47	2.51±0.32
	SEB	3.84±0.69	3.90±0.56	3.37±0.16	3.82±0.59
C_{osm}, ml/min/kg	Controls	0.34±0.06	0.35±0.01	0.36±0.04	0.38±0.01
	SEB	0.40±0.06	0.33±0.02	0.35±0.02	0.38±0.02
$T^{C}_{H_2O}$, ml/min/kg	Controls	0.16±0.02	0.17±0.02	0.17±0.02	0.16±0.01
	SEB	0.17±0.01	0.16±0.02	0.17±0.01	0.17±0.01
Tm_{PAH}, ml/min/kg	Controls	5.06±0.42	5.34±0.32	4.97±0.39	4.94±0.24
	SEB	4.85±0.48	4.84±0.47	4.44±0.69	4.94±0.55
Urine flow, ml/min	Controls	0.82±0.15	0.92±0.18	0.95±0.17	0.85±0.08
	SEB	0.98±0.07	1.02±0.06	0.97±0.06	0.99±0.05

Figures

Fig. 1. Effect of iv SEB on mean arterial blood pressure and heart rate in rhesus monkeys.

Fig. 2. Effect of iv SEB on cardiac output, stroke volume, total peripheral resistance and cardiac work in rhesus monkeys.

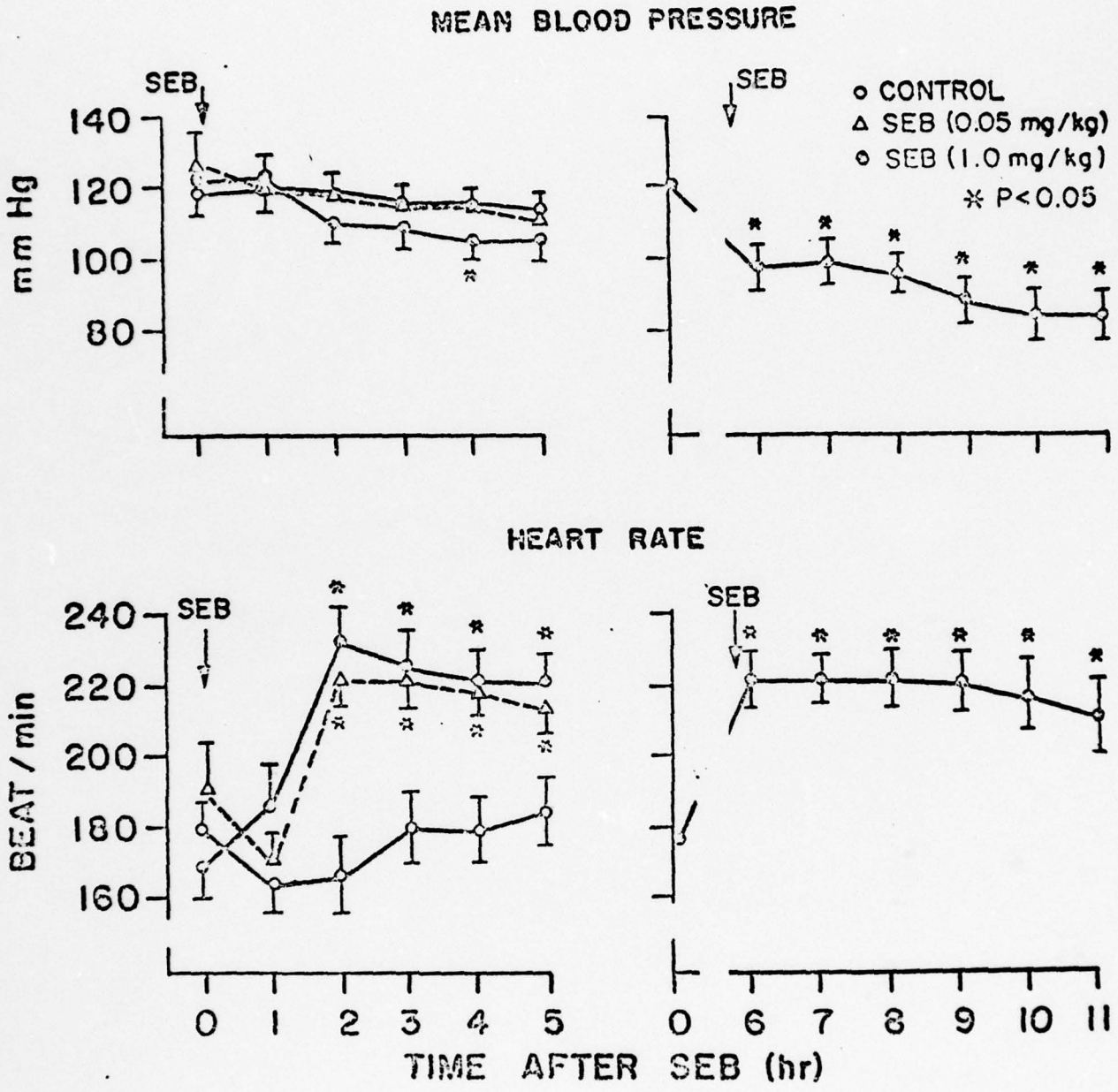
MEAN BLOOD PRESSURE
SEB
SEB
o CONTROL
Δ SEB (0.05 mg/kg)
o SEB (1.0 mg/kg)
* P<0.05
mm Hg
140
120
100
80
HEART RATE
SEB
SEB
BEAT / min
240
220
200
180
160
0 1 2 3 4 5
0 6 7 8 9 10 11
TIME AFTER SEB (hr)

Fig. 1

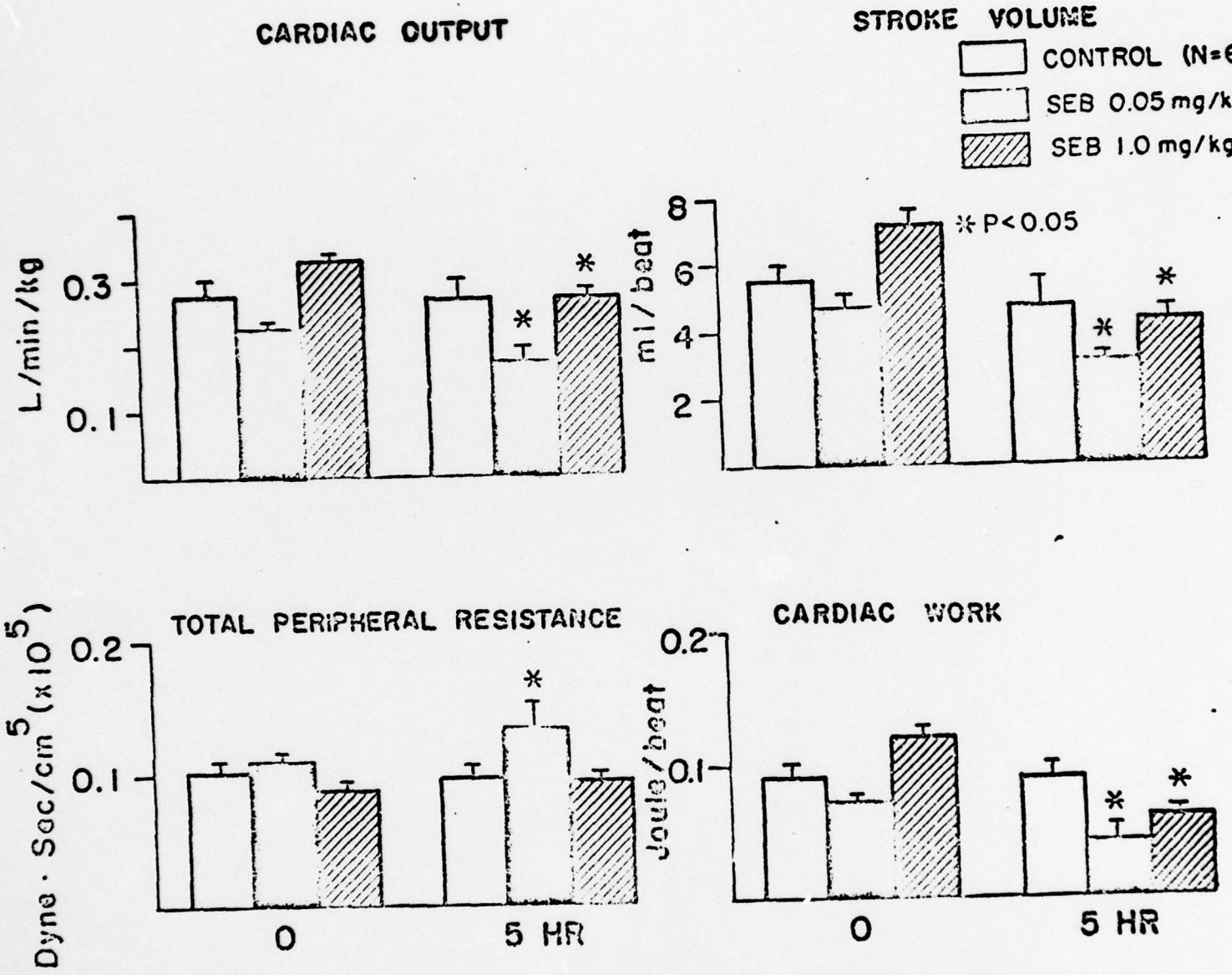
CARDIAC OUTPUT
L/min/kg
0.3
0.1
STROKE VOLUME
CONTROL (N=6)
SEB 0.05 mg/kg (N=7)
SEB 1.0 mg/kg (N=8)
ml/beat
8
6
4
2
* P<0.05
TOTAL PERIPHERAL RESISTANCE
Dyne · Sec/cm^5 (x10^5)
0.2
0.1
CARDIAC WORK
Joule/beat
0.2
0.1
0
5 HR
0
5 HR

Fig. 2